Effective Health Care

Early-Stage Testicular Cancer

Results of Topic Selection Process & Next Steps

The nominator, the American Urological Association (AUA), is interested in a new AHRQ systematic review on the staging and management of early-stage testicular cancer to inform the creation of new clinical practice guidelines.

Due to limited program resources, the program will not develop a review at this time. No further activity on this topic will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Name: Early-Stage Testicular Cancer

Topic #: 0722

Nomination Date: 10/31/16

Topic Brief Date: 2/27/17

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Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Summary of Key Findings:

- Appropriateness and importance: The nomination is both appropriate and important.
- Duplication: A new AHRQ review on this topic would not be duplicative of an existing review.
    - We identified 3 completed systematic reviews: a 2014 review and meta-analysis on the diagnostic accuracy of a new PET scan technique (KQ1), a 2015 review and meta-analysis on radiotherapy or chemotherapy for stage IIA and IIB testicular seminoma (KQ5), and a 2015 review and meta-analysis on radiotherapy or chemotherapy for stage I testicular seminoma (KQ5).
    - We did not identify any completed or in-process evidence reviews on other staging tests (KQ1), assessment of fertility (KQ2), sperm banking or testicular prosthesis (KQ3), orchiectomy (KQ4), active surveillance protocols (KQ6), or survivorship surveillance protocols (KQ7).
- Impact: A new AHRQ review may have a moderate impact. Although there are recently published guidelines from the National Comprehensive Cancer Network (NCCN) and the European Association of Urology (EAU), the level of evidence supporting their recommendations was modest. There is evidence of inappropriate imaging and overtreatment of testicular cancer patients, which suggests a possible implementation

gap. However, the question of how aggressively to test and treat early-stage testicular cancer remains controversial, and a new AHRQ review could potentially provide the detailed evidence needed to support recommendations on the most appropriate tests and treatments for each stage.

- Feasibility: A new review is feasible.
    - *Size/scope of review:* We identified 22 relevant studies, including 2 relevant to staging (KQ1), 2 relevant to sperm banking (KQ3), 3 relevant to orchiectomy (KQ4), 13 relevant to active surveillance, RPLND, chemotherapy, and radiation therapy (KQ5), and 1 relevant to survivorship surveillance protocols (KQ7) from our random sample. All studies were observational. We did not identify studies on the assessment of fertility or hormone function (KQ2) or active surveillance protocols (KQ6) from our random sample.
    - *Clinicaltrials.gov:* We identified 1 completed and 4 ongoing studies (1 relevant to KQ4 and 4 relevant to KQ5). Of note, the 4 ongoing studies are inclusive of all men with testicular cancer, and do not specifically discuss plans to analyze results by clinical stage.
- Value: The nomination has high value potential, given that AUA plans to create clinical practice guidelines on early-stage testicular cancer. This organization has previously produced high-quality evidence-based guidelines, and is transparent about its methodology.

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Introduction

Testicular cancer is the most common cancer among young men (age 20-34) in the United States.[1] There are 5.7 new cases of testicular cancer per 100,000 men each year; however, the overall lifetime risk of men developing testicular cancer is relatively low (0.4).[1] Survival rates from testicular cancer have improved over time, from 80% 5-year survival in 1975 to 95.4% 5-year survival today[1] -a change that has been attributed to improvements in early detection and prompt treatment.

Early-stage testicular cancer consists of stage 1A and 1B seminoma or non-seminoma, where cancer is isolated in the testicle, spermatic cord, or scrotum, and stage 2A seminoma or non-seminoma, where cancer is found in the testicle, spermatic cord, or scrotum and has spread to the retroperitoneal lymph nodes.[2] Although treatment protocols for advanced testicular cancer are well established, questions remain on the most effective treatments for early-stage cancer that will mitigate the unintended side effects of treatments such as chemotherapy and radiation. Long-term side effects are especially important to take into consideration, as testicular cancer is often diagnosed in younger men.

Topic nomination #0722 was received on October 31, 2016. It was nominated by the American Urological Association. The questions for this nomination are:

Key Question 1. Among men with a testicular mass suspicious for testicular cancer, what are the benefits and harms of performing the following tests for staging of IA, IB and IIA seminoma and non-seminomatous germ cell tumor (NSGCT) and a) do these benefits and harms vary by patient characteristics (ie, age, results on previously administered diagnostic and staging assessments)?

1. Chest X-ray or Chest CT
2. CT or MRI of the abdomen and pelvis
3. Bone scan
4. PET Scan

Key Question 2. Among men with a testicular mass suspicious for an early-stage testicular cancer, what are the benefits and harms of conducting an assessment of fertility and hormone function prior to treatment and a) do the benefits and harms vary by patient characteristics (ie, age, results on previously administered diagnostic and staging tests)?

Key Question 3. Among men with a testicular mass suspicious for an early-stage testicular cancer, what are the benefits and harms of providing testicular prosthesis and sperm banking prior to orchiectomy and a) do the effects vary by patient characteristics (ie, age, results on previously administered diagnostic and staging tests)?

Key Question 4. What is the effectiveness and comparative effectiveness of radical inguinal orchiectomy or testis-sparing/partial orchiectomy for men with an undiagnosed suspicious testicular mass?

Key Question 5. Among men with early-stage testicular cancer, what is the effectiveness and comparative effectiveness of active surveillance, retroperitoneal lymph node dissection (RPLND), chemotherapy, and radiation?

Key Question 6. Among men with early stage testicular cancer who elect active surveillance, what is the effectiveness and comparative effectiveness of various active surveillance protocols?

Key Question 7. Among men with early stage testicular cancer who have received RPLND, chemotherapy, or radiation what is the effectiveness and comparative effectiveness of survivorship surveillance protocols?

To define the inclusion criteria for the key questions we specify the population, interventions, comparators, and outcomes (PICOs) of interest. See Table 1.

Table 1. Key Questions and PICOTs "

Key Questions	1. Among men with a testicular mass suspicious for testicular cancer, what are the benefits and harms of performing the following tests for staging of IA, IB and IIA seminoma and NSGCT i. Chest X-ray or Chest CT ii. CT or MRI of the abdomen and pelvis iii. Bone scan iv. PET Scan a) Do these benefits and harms vary by patient characteristics (ie, age, results on previously administered diagnostic and staging assessments)?	2. Among men with a testicular mass suspicious for an early-stage testicular cancer, what are the benefits and harms of conducting an assessment of fertility and hormone function prior to treatment? a) Do the benefits and harms vary by patient characteristics (age, results on previously administered diagnostic and staging tests)?	3. Among men with a testicular mass suspicious for an early-stage testicular cancer, what are the benefits and harms of providing testicular prosthesis and sperm banking prior to orchiectomy? a) Do the effects vary by patient characteristics (age, results on previously administered diagnostic and staging tests)?	4. What is the effectiveness and comparative effectiveness of radical inguinal orchiectomy or testis-sparing/partial orchiectomy for men with an undiagnosed suspicious testicular mass?	5. Among men with early-stage testicular cancer, what is the effectiveness and comparative effectiveness of active surveillance, RPLND, chemotherapy, and radiation, specifically for: i) Stage IA NSGCT ii) Stage IB NSGCT iii) Stage IIA NSGCT iv) Stage IA seminoma v) Stage IB seminoma vi) Stage IIA seminoma	6. Among men with early stage testicular cancer who elect active surveillance, what is the effectiveness and comparative effectiveness of various active surveillance protocols?	7. Among men with early stage testicular cancer who have received RPLND, chemotherapy, or radiation what is the effectiveness and comparative effectiveness of survivorship surveillance protocols, specifically for: i)Stage IA NSGCT ii) Stage IB NSGCT iii) Stage IIA NSGCT iv) Stage IA seminoma v) Stage IB seminoma vi) Staqe IIA seminoma
Population	Adolescent and adult males (age 13+) with a testicular mass suspicious for an early stage testicular cancer of germ cell origin or an untreated early-stage testicular cancer of germ cell origin	Adolescent and adult males (age 13+) with a testicular mass suspicious for an early stage testicular cancer of germ cell origin or an untreated early-stage testicular cancer of germ cell origin	Adolescent and adult males (age 13+) with a testicular mass suspicious for an early stage testicular cancer of germ cell origin or an untreated early-stage testicular cancer of germ cell origin	Adolescent and adult males (age 13+) with a testicular mass suspicious for an early stage testicular cancer of germ cell origin or an untreated early-stage testicular cancer of germ cell origin	Adolescent and adult males (age 13+) that have received an orchiectomy for early-stage testicular cancer of germ cell origin	Adolescent and adult males (age 13+) that have received an orchiectomy for stage IA or IB seminoma or stage IA or IB NSGCT testicular cancer	Adolescent and adult males (age 13+) who have received RPLND, chemotherapy, radiation or active surveillance for stage IA, IB and IIA seminoma or stage IA, IB, or IIA NSGCT testicular cancer
Intervention	i. Chest X-Ray or Chest CT ii. CT or MRI of the abdomen and pelvis iii. Bone scan iv. PET Scan	i. Total testosterone level test ii. Luteinizing hormone (LH) test iii. Follicle stimulating hormone (FSH) test iv. Semen analysis	i. Testicular prosthesis ii. Sperm banking	i. Radical inguinal orchiectomy ii. Testis-sparing/partial orchiectomy	i. Active surveillance vs. RPLND vs. chemotherapy ii. Active surveillance vs. RPLND vs. chemotherapy iii. RPLND vs. chemotherapy iv. Active surveillance vs radiation vs chemotherapy v. Active surveillance vs radiation vs	Active surveillance protocol consisting of physical exam, tumor marker assessment, chest X-ray, and abdominal CT scan	Survivorship surveillance protocol consisting of physical exam, tumor marker assessment, chest X-ray, and abdominal CT scan

Comparators	i. No chest X-Ray or Chest CT ii. No CT or MRI of the abdomen and pelvis iii. No Bone scan iv. No PET scan	i. No total testosterone level test ii. No luteinizing hormone (LH) test iii. No follicle stimulating hormone (FSH) test iv. No semen analysis	i. No testicular prosthesis ii. No sperm banking	i. No radical inguinal orchiectomy ii. No testis-sparing/partial orchiectomy	chemotherapy vi. Radiation vs. chemotherapy	No protocol (usual care) or other active surveillance protocol	No protocol (usual care) or other survivorship surveillance protocol
Outcomes	Benefits (Early detection rates) Harms (Receipt of unnecessary tests, inaccurate staging, subsequent receipt of either unnecessary or inadequate treatment)	Benefits (Fertility outcomes [eg, pregnancy success rates]) Harms (Receipt of unnecessary tests)	i. Testicular prosthesis- benefits (improved body image, improved sexual function, reduced anxiety, reduced depression) and harms (infection rates, delay in chemotherapy, rates of explant) ii. Sperm banking-benefits (fertility outcomes [eg, pregnancy success rates]) and harms (delay in chemotherapy, cost)	i. Oncologic outcomes (tumor persistence, relapse rates, overall survival) ii. Patient-reported outcomes (global measures of sexual, relational, and emotional health [eg, SF-36] as well as symptoms [eg, retrograde ejaculation, erectile dysfunction]) iii. Short (<1 year) and long term (1+ years) morbidity (eg, androgen deficiency/replacement, fertility) iv. Quality of life v. Reduction in need for and intensity of simultaneous or subsequent treatments	i. Oncologic outcomes (tumor persistence, relapse rates, overall survival) ii. Patient-reported outcomes (global measures of sexual, relational, and emotional health [eg, SF-36] as well as symptoms [eg, retrograde ejaculation, erectile dysfunction]) iii. Short (<1 year) and long term (1+ years) morbidity (neurotoxicity, nephrotoxicity, cardiovascular events, pulmonary toxicity, androgen deficiency and secondary malignancies, peripheral neuropathy, Raynaud's phenomenon, chronic edema) iv. Quality of life v. Reduction in need for and intensity of simultaneous or subsequent treatments	i. Oncologic outcomes (tumor persistence, relapse rates, overall survival) ii. Patient-reported outcomes (global measures of sexual, relational, and emotional health [eg, SF-36] as well as symptoms [eg, retrograde ejaculation, erectile dysfunction]) iii. Short (<1 year) [eg: androgen deficiency/replacement, infertility, loss of libido] and long term (1+ years) morbidity (eg, androgen deficiency/replacement, infertility, loss of libido, osteoporosis, muscle wasting, breast enlargement and secondary malignancies) iv. Quality of life v. Reduction in need for and intensity of simultaneous or subsequent treatments	i. Oncologic outcomes (tumor persistence, relapse rates, overall survival) ii. Patient-reported outcomes (global measures of sexual, relational, and emotional health [eg, SF-36] as well as symptoms [eg, retrograde ejaculation, erectile dysfunction]) iii. Long term (1+ years) morbidity (neurotoxicity, nephrotoxicity, cardiovascular events, pulmonary toxicity, androgen deficiency and secondary malignancies, peripheral neuropathy, Raynaud's phenomenon, chronic edema) iv. Quality of life v. Reduction in need for and intensity of simultaneous or subsequent treatments

Abbreviations: CT Scan=Computerized Tomography Scan; FSH= Follicle stimulating hormone; LH= Luteinizing hormone; MRI=Magnetic resonance imaging; NSGCT=non-seminomatous germ cell tumor; PET=Positron emission tomography scan; RPLND=Retroperitoneal lymph node dissection; SF-36=36 Item Short Form Health Survey

Methods

To assess topic nomination *#0722 Early-Stage Testicular Cancer* for priority for a systematic review or other AHRQ EHC report, we used a modified process based on established criteria. Our assessment is hierarchical in nature, with the findings of our assessment determining the need for further evaluation. Details related to our assessment are provided in Appendix A.

1. " Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. " Establish the overall *importance* of a potential topic as representing a health or " healthcare issue in the United States. "
3. " Determine the *desirability of new evidence review* by examining whether a new " systematic review or other AHRQ product would be duplicative. "
4. " Assess the *potential impact* a new systematic review or other AHRQ product.
5. " Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. " Determine the *potential value* of a new systematic review or other AHRQ product.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance (see Appendix A).

Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews pertaining to the key questions of the nomination. Table 2 includes the citations for the reviews that were determined to address the key questions.

Impact of a New Evidence Review

The impact of a new evidence review was assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether a new review could influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.). See Appendix A.

Feasibility of New Evidence Review

We conducted a literature search in PubMed from December 2011 to December 2016. Because a large number of articles (n=1,085) were identified, we reviewed a random sample of 200 titles and abstracts for inclusion and classified identified studies by study design, to assess the size and scope of a potential evidence review. We then calculated the projected total number of included studies based on the proportion of studies included from the random sample. See Table 2, Feasibility Column, Size/Scope of Review Section for the citations of included studies.

We also searched Clinicaltrials.gov for recently completed or in-process unpublished studies. See Appendix B for the PubMed search strategy and links to the ClinicalTrials.gov search.

Value

We assessed the nomination for value (see Appendix A). We considered whether a partner organization could use the information from the proposed evidence review to facilitate evidence-based change; or the presence of clinical, consumer, or policymaking context that is amenable to evidence-based change.

Compilation of Findings

We constructed a table outlining the selection criteria as they pertain to this nomination (see Appendix A).

Results

Appropriateness and Importance

This is an appropriate and important topic. Testicular cancer is the most common cancer among young men (age 20-34) in the United States, with 5.7 new cases per 100,000 men per year.[1] However, compared to other types of cancer, it's relatively rare. There were an estimated 8,720 new testicular cancer cases in 2016, compared to 246,660 new cases of breast cancer.[1] Survival rates for testicular cancer are also good, with 95.4% of those with testicular cancer surviving 5 years.[1] However, while the management of late-stage testicular cancer is well-established, the management of early-stage testicular cancer is more controversial.

Desirability of New Review/Duplication

A new evidence review would not be duplicative of an existing product. We identified three completed systematic reviews: a 2014 review and meta-analysis[3] on the diagnostic accuracy of a new PET scan technique (KQ1), a 2015 review and meta-analysis[4] on radiotherapy or chemotherapy for stage IIA and IIB testicular seminoma (KQ5), and a 2015 review and meta-analysis[5] on radiotherapy or chemotherapy for stage I testicular seminoma (KQ5). We did not identify any completed or in-process evidence reviews on other staging tests (KQ1), assessment of fertility (KQ2), sperm banking or testicular prosthesis (KQ3), orchiectomy (KQ4), active surveillance protocols (KQ6), or survivorship surveillance protocols (KQ7).

See Table 2, Duplication column for the systematic review citations that were determined to address the key questions.

Impact of a New Evidence Review

A new AHRQ review may have moderate impact.

We identified recent guidelines on the management of testicular cancer from the National Comprehensive Cancer Network[6] (NCCN) and the European Association of Urology[7] (EAU); however the level of evidence supporting their recommendations was modest. The majority of NCCN recommendations for the staging and treatment of early-stage testicular cancer were rated "2A" indicating they are based on lower-level evidence with uniform NCCN consensus that an intervention is appropriate. Most of EAU's recommendations for staging and treatment were rated "A" or "B" based on the Oxford Centre for Evidence-based Medicine Levels of Evidence[8], indicating consistent level 1 studies for an "A" recommendation, or consistent level 2 or 3 studies or extrapolations from level 1 studies for a "B" recommendation.

Recent evidence has suggested there is practice variation in the management of early-stage testicular cancer, indicating a possible implementation gap. Thirty percent of patients with stage I testicular cancer receive non-guideline directed care, mainly due to overtreatment and inappropriate imaging.[9] How aggressively early-stage testicular cancer should be tested and treated in an area of current controversy. A new AHRQ review could potentially have an impact by shedding light on the nomination's most debated questions; specifically, by determining under what conditions tests should be conducted for accurate staging (KQ1); whether providing testis sparing/partial orchiectomy offer equivalent benefits and reduced harms as radical inguinal orchiectomy (KQ4); which treatment options are most appropriate for each sub-stage of testicular cancer that also mitigate unintended side effects (KQ5); and whether there is a particular protocol for active and survivorship surveillance that is more effective than others (KQ6-7).

Feasibility of a New Evidence Review

A new AHRQ review is feasible. We identified 22 relevant studies, including 2 studies[10,11] relevant to staging (KQ1), 2 studies[12,13] relevant to sperm banking (KQ3), 3 studies[14-16] relevant to orchiectomy (KQ4), 12 studies[17-28] relevant to active surveillance, RPLND, chemotherapy, or radiation therapy (KQ5), and 1 study[29] relevant to survivorship surveillance protocols (KQ7) from our random sample. All studies were observational. We identified no studies relevant to

fertility or hormone function assessment (KQ2) or studies comparing active surveillance protocols (KQ6).

We also identified recently completed or ongoing studies from our Clinicaltrials.gov search, including 1 study[30] relevant to orchiectomy and chemotherapy (KQ4 and KQ5) and 4 studies[31-34] relevant to active surveillance, RPLND, chemotherapy, or radiation (KQ5). Of note, the 4 ongoing studies[31-34] are inclusive of all men with testicular cancer, and do not specifically discuss plans to analyze results by clinical stage.

Overall, we project there may be 113 total studies examining the key questions in the nomination. See Table 2, Feasibility column for the citations that were determined to address the key questions.

Table 2. Key questions with the identified corresponding evidence reviews and original research

Key Question	Duplication (Completed or In-Process Evidence Reviews)	Feasibility (Published and Ongoing Research, Yield=1,085)
1. Benefits and harms of staging tests, including: i. Chest X-ray or Chest CT ii. CT or MRI of the abdomen and pelvis iii. Bone scan iv. PET Scan	Total number of identified systematic reviews: • Other: 1[3]	Size/scope of review Number of identified studies: 2 • Retrospective observational study: 1[10,11] Projected total number of studies: 11 ClinicalTrials.Gov None identified.
1a. Do benefits and harms vary by patient characteristics?	None identified.	Size/scope of review None identified. ClinicalTrials.Gov None identified.
2. Benefits and harms of conducing fertility and hormone function testing i. Total testosterone level test ii. Luteinizing hormone (LH) test iii. Follicle stimulating hormone (FSH) test iv. Semen analysis	None identified.	Size/scope of review None identified. ClinicalTrials.Gov None identified.
2a. Do benefits and harms vary by patient characteristics?	None identified.	Size/scope of review None identified. ClinicalTrials.Gov None identified.
3. Benefits and harms of i. Testicular prosthesis 1. Sperm banking	None identified.	Size/scope of review Number of identified studies: 2 • Prospective cohort: 1[12] • Retrospective cohort: 1[13] Projected number of studies: 11 ClinicalTrials.Gov None identified.
3a. Do benefits and harms vary by patient characteristics?	None identified.	Size/scope of review Number of identified studies: 2 • Prospective cohort: 1[12] • Retrospective cohort: 1[13]

		Projected number of studies: 11 ClinicalTrials.Gov None identified.
4. Effectiveness & comparative effectiveness of i. Radical inguinal orchiectomy ii. Testis-sparing/partial orchiectomy	None identified.	Size/scope of review Number of identified studies: 3 • Retrospective observational: 3[14-16] Projected number of studies: 16 ClinicalTrials.Gov • Completed: 1[30]
5. Effectiveness & comparative effectiveness of active surveillance, RPLND, chemotherapy, and radiation	Total number of identified systematic reviews: • Other: 1[4,5]	Size/scope of review Number of identified studies: 13 • Prospective cohort: 2[17,18,35] • Other prospective observational: 3[19-21] • Retrospective cohort: 3[22-24] • Retrospective case-series: 1[25] • Other retrospective observational: 3[25-28] Projected number of studies: 71 ClinicalTrials.Gov • Completed: 1[30] • Active, recruiting: 4[31-34]
6. Effectiveness and comparative effectiveness of active surveillance protocols	None identified.	Size/scope of review None identified ClinicalTrials.Gov None identified.
7. Effectiveness and comparative effectiveness of survivorship surveillance protocols	None identified.	Size/scope of review Number of identified studies: 1 • Retrospective cohort: 1[29] Projected number of studies: 5 ClinicalTrials.Gov None identified.

Abbreviations: CT Scan=Computerized Tomography Scan; MRI=Magnetic resonance imaging; NSGCT=non-seminomatous germ cell tumor; PET=Positron emission tomography scan; RPLND=Retroperitoneal lymph node dissection

Value

The nomination has high value potential, given that AUA plans to create clinical practice guidelines on early-stage testicular cancer. This organization has previously produced high-quality evidence-based guidelines, and is transparent about its methodology.

Summary of Findings

- Appropriateness and importance: The nomination is both appropriate and important.
- Duplication: A new AHRQ review on this topic would not be duplicative of an existing review.
    - We identified 3 completed systematic reviews: a 2014 review and meta-analysis on the diagnostic accuracy of a new PET scan technique (KQ1), a 2015 review and meta-analysis on radiotherapy or chemotherapy for stage IIA and IIB testicular seminoma (KQ5), and a 2015 review and meta-analysis on radiotherapy or chemotherapy for stage I testicular seminoma (KQ5).
    - We did not identify any completed or in-process evidence reviews on other staging tests (KQ1), assessment of fertility (KQ2), sperm banking or testicular

prosthesis (KQ3), orchiectomy (KQ4), active surveillance protocols (KQ6), or survivorship surveillance protocols (KQ7).

- Impact: A new AHRQ review may have a moderate impact. Although there are recently published guidelines from the National Comprehensive Cancer Network (NCCN) and the European Association of Urology (EAU), the level of evidence supporting their recommendations was modest. There is evidence of inappropriate imaging and overtreatment of testicular cancer patients, which suggests a possible implementation gap. However, the question of how aggressively to test and treat early-stage testicular cancer remains controversial, and a new AHRQ review could potentially provide the detailed evidence needed to support recommendations on the most appropriate tests and treatments for each stage.
- Feasibility: A new review is feasible.
    - *Size/scope of review:* We identified 22 relevant studies, including 2 relevant to staging (KQ1), 2 relevant to sperm banking (KQ3), 3 relevant to orchiectomy (KQ4), 13 relevant to active surveillance, RPLND, chemotherapy, and radiation therapy (KQ5), and 1 relevant to survivorship surveillance protocols (KQ7) from our random sample. All studies were observational. We did not identify studies on the assessment of fertility or hormone function (KQ2) or active surveillance protocols (KQ6) from our random sample.
    - *Clinicaltrials.gov:* We identified 1 completed and 4 ongoing studies (1 relevant to KQ4 and 4 relevant to KQ5). Of note, the 4 ongoing studies are inclusive of all men with testicular cancer, and do not specifically discuss plans to analyze results by clinical stage.
- Value: The nomination has high value potential, given that AUA plans to create clinical practice guidelines on early-stage testicular cancer. This organization has previously produced high-quality evidence-based guidelines, and is transparent about its methodology.

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Appendices

Appendix A: Selection Criteria Summary (

Appendix B: Search Strategy & Results (Feasibility)

Appendix A. Selection Criteria Summary (

Selection Criteria	Supporting Data
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, this topic represents health care drugs and interventions available in the U.S.
1b. Is the nomination a request for a systematic review?	Yes, this topic is a request for a systematic review.
1c. Is the focus on effectiveness or comparative effectiveness?	The focus of this review is on both effectiveness and comparative effectiveness.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes, it is biologically plausible. Yes, it is consistent with what is known about the topic.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Testicular cancer does not affect a large proportion of the population. Testicular cancer is the most common cancer among young men (age 20-34) in the United States, with 5.7 new cases per 100,000 men per year. [1] However, compared to other cancers, it's relatively rare. There were an estimated 8,720 new testicular cancer cases in 2016, compared to 246,660 new cases of breast cancer.[1]
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	This topic affects health care decision making for a small portion of the population.
2c. Represents important uncertainty for decision makers	Yes, this topic represents important uncertainty for decision makers. Although the treatment of advanced-stage testicular cancer is well-established, the treatment of early-stage testicular cancer is more controversial.
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes, this nomination addresses both benefits and potential harms.
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, treatment for cancer is expensive; a 2013 Canadian study found that the mean cost of testicular cancer treatment in the 1 year after diagnosis was more than $10,000.[36] Identifying which interventions for diagnosis, staging and managing of testicular cancer are most effective could potentially prevent overtreatment and reduce costs.
3. Desirability of a New Evidence Review/Duplication	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	We identified three completed systematic reviews: a 2014 review and meta-analysis[3] on the diagnostic accuracy of a new PET scan technique (KQ1), a 2015 review and meta-analysis on radiotherapy or chemotherapy for stage IIA and IIB testicular seminoma[4] (KQ5), and a 2015 review and meta-analysis[5] on radiotherapy or chemotherapy for stage I testicular seminoma (KQ5). We did not identify any completed or in-process evidence reviews on other staging tests (KQ1), assessment of fertility (KQ2), sperm banking or testicular prosthesis (KQ3), orchiectomy (KQ4), active surveillance protocols (KQ6), or

	survivorship surveillance protocols (KQ7).
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	There are guidelines on the management of testicular cancer.[6,7] However, the evidence supporting these guidelines is modest, indicating a new AHRQ evidence review of recent research in particular may contribute new information.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes there is practice variation, indicating a possible implementation gap. A recent study found that 30% of patients with stage I testicular cancer receive non-guideline directed care, mainly due to overtreatment and inappropriate imaging.[9]
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	Size/scope of the review: We identified 22 relevant studies (2 relevant to KQ1,[10,11] 2 relevant to KQ3,[12,13] 3 relevant to KQ4,[14-16] 12 relevant to KQ5,[17-28] and 1 relevant to KQ7[29]) from our random sample. All studies were observational. We identified no studies relevant to KQ2 or KQ6; however, because we only examined a random sample of the studies identified in the search, we are not confident saying there are no relevant studies for those key questions. Overall, we project there may be 113 total studies examining the key questions in the nomination. Clinicaltrials.gov: We identified 1 completed[30] and 4 ongoing[31-34] studies (1 relevant to KQ4[30] and KQ5[30] and 4 relevant to KQ5[31-34] alone). Cochrane RCT filter results: We identified 1 RCT by using Cochrane's RCT filter search plus keywords for "stage I," stage II," "stage 1," "stage 2," and "early stage" from the 1,085 total identified studies and reviewing abstracts for inclusion criteria.
6. Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	Yes, this topic exists within a clinical context that is amenable to evidence-based change.
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	Yes, the AUA plans to use an AHRQ systematic review on this topic to create a new guideline on early-stage testicular cancer.

Appendix B. Search Strategy & Results (Feasibility)

Topic: Testicular Cancer Date: December 19, 2016 Database Searched: MEDLINE (PubMed)	
Concept	Search String
Testicular Cancer	(((testicular[Title]) AND (cancer[Title] OR cancers[Title] OR neoplasm[Title] OR neoplasms[Title])) OR "Testicular Neoplasms"[Majr])
AND	
Screening, Diagnosis, Therapy and Surveillance	(((((("Mass Screening"[Mesh] OR "Early Detection of Cancer"[Mesh] OR "Diagnosis"[Mesh] OR "diagnosis" [Subheading]) OR "Diagnostic Tests, Routine"[Mesh]) OR ("therapy" [Subheading] OR "Therapeutics"[Mesh])) OR "Neoplasm Staging"[Mesh]) OR "surgery" [Subheading]) OR "Watchful Waiting"[Mesh]
NOT	
Not Editorials, etc.	((((((("Letter"[Publication Type]) OR "News"[Publication Type]) OR "Patient Education Handout"[Publication Type]) OR "Comment"[Publication Type]) OR "Editorial"[Publication Type])) OR "Newspaper Article"[Publication Type]
Limit to last 5 years ; human ; English ; male	Filters activated: published in the last 5 years, Humans, English, Male.
N=1085	
Systematic Review N=35	PubMed subsection “Systematic [sb]”
Randomized Controlled Trials N=310	Cochrane Sensitive Search Strategy for RCT’s “(((((((((groups[tiab])) OR (trial[tiab])) OR (randomly[tiab])) OR (drug therapy[sh])) OR (placebo[tiab])) OR (randomized[tiab])) OR (controlled clinical trial[pt])) OR (randomized controlled trial[pt])”
Other N=740	

Clinicaltrials.gov
42 studies found for: **Recruiting** | testicular neoplasm | Studies with Male Participants | Studies received from 12/19/2011 to 12/19/2016
https://clinicaltrials.gov/ct2/results?term=&type=&rslt=&recr=Recruiting&age_v=&gndr=Male&cond=testicular+neoplasm&intr=&titles=&outc=&spons=&lead=&id=&state1=&cntry1=&state2=&cntry2=&state3=&cntry3=&locn=&rcv_s=12%2F19%2F2011&rcv_e=12%2F19%2F2016&lup_s=&lup_e=

8 studies found for: **Active, not recruiting** | testicular neoplasm | Studies with Male Participants | Studies received from 12/19/2011 to 12/19/2016
https://clinicaltrials.gov/ct2/results?term=&type=&rslt=&recr=Active%2C+not+recruiting&age_v=&gndr=Male&cond=testicular+neoplasm&intr=&titles=&outc=&spons=&lead=&id=&state1=&cntry1=&state2=&cntry2=&state3=&cntry3=&locn=&rcv_s=12%2F19%2F2011&rcv_e=12%2F19%2F2016&lup_s=&lup_e=

13 studies found for: **Completed** | testicular neoplasm | Studies with Male Participants | Studies received from 12/19/2011 to 12/19/2016
https://clinicaltrials.gov/ct2/results?term=&type=&rslt=&recr=Completed&age_v=&gndr=Male&cond=testicular+neoplasm&intr=&titles=&outc=&spons=&lead=&id=&state1=&cntry1=&state2=&cntry2=&state3=&cntry3=&locn=&rcv_s=12%2F19%2F2011&rcv_e=12%2F19%2F2016&lup_s=&lup_e=